Notice of Allowability	Application No.	Applicant(s)	
	10/099,700	MADISON ET AL.	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed 10 November 3005 and the interview conducted 20 January 2006*.

2. ☒ The allowed claim(s) is/are *1,2,4,5,8,9,18,50-53,59-61,65-67,69-79,82 and 123-128*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

The numbering of several of the new claims submitted with the amendment filed 10 November 2005 is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims beginning with the second claim 125 through the claim numbered 127 have been renumbered as claims 126-128.

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Delete claims 80, 81, and 87-116.

Amend claims 1, 4, 5, 8, 9, 18, 50-53, 59-61, 65, 67, 69-74, 76-79, 123-125, and the renumbered claims 126-128 thus:

1. (Amended) A substantially purified single or two chain MTSP7 protease ~~polypeptide or a catalytically active portion of the polypeptide, wherein the polypeptide~~ that comprises the ~~a~~ sequence of amino acids encoded by the sequence of nucleotides set forth in SEQ ID No. 15.

4. (Amended) A substantially purified ~~single or~~ two chain protease ~~polypeptide~~, comprising the ~~an~~ MTSP7 protease domain ~~or comprising a catalytically active fragment thereof, wherein: said MTSP; protease domain or catalytically active fragment thereof is the only MTSP7 portion of the single or two chain polypeptide and the protease domain of MTSP7 has only the sequence of amino acid residues~~ encoded by the sequence of nucleotides set forth in SEQ ID No. 17.

5. (Amended) A ~~The~~ substantially purified ~~polypeptide of claim 1, wherein the MTSP7 is a human polypeptide~~ single chain or two chain protease that consists of the MTSP7 protease domain encoded by the sequence of nucleotides set forth in SEQ ID No. 17.

8. (Amended) The substantially purified protease ~~polypeptide~~ of claim 1 that comprises the sequence of amino acids set forth in SEQ ID No. 16.

9. (Amended) The substantially purified protease ~~polypeptide~~ of claim 5 ~~4~~ that ~~comprises~~ consists of the sequence of amino acids set forth in SEQ ID No. 18.

18. (Amended) A ~~substantially purified~~ modified single or two chain MTSP7 protease ~~polypeptide or a catalytically active portion of the polypeptide,~~ wherein the protease ~~polypeptide that~~ comprises the ~~a~~ sequence of amino acids encoded by the sequence of nucleotides set forth in SEQ ID No. 15~~,~~ modified by the replacement of ~~except that~~ a free Cysteine in the protease domain ~~is replaced~~ with another amino acid.

50. (Amended) A conjugate~~,~~ comprising~~:~~ the protease ~~a polypeptide~~ of claim 1~~,~~ or claim 5 and a targeting agent linked to the protease ~~polypeptide~~ directly or via a linker.

51. (Amended) The conjugate of claim 50, wherein the targeting agent permits affinity isolation or purification of the conjugate~~,~~ attachment of the conjugate to a surface~~,~~ detection of the conjugate~~,~~ or targeted delivery of the conjugate to a selected tissue or cell.

52. (Amended) A conjugate, comprising~~:~~ the protease ~~a polypeptide~~ of claim 4, and a targeting agent linked to the protease ~~polypeptide~~ directly or via a linker.

53. (Amended) The conjugate of claim 52, wherein the targeting agent permits affinity isolation or purification of the conjugate~~,~~ attachment of the conjugate to a surface~~,~~

detection of the conjugate, ~~;~~ or targeted delivery of the conjugate to a selected tissue or cell.

59. (Amended) A solid support, comprising two or more proteases ~~polypeptides~~ of claim 1 or claim 5 linked thereto either directly or via a linker.

60. (Amended) The support of claim 59, wherein the proteases ~~polypeptides~~ comprise an array.

61. (Amended) The array ~~support~~ of claim ~~59~~ 60, wherein the array ~~polypeptides~~ further comprises ~~comprise~~ a plurality of different protease domains.

65. (Amended) A method for identifying compounds that inhibit the protease activity of the protease of claim 1 or claim 5 ~~a polypeptide~~, comprising:

contacting the protease of claim 1 or claim 5 ~~a polypeptide of claim 1~~ with a substrate that is proteolytically cleaved by the protease ~~polypeptide~~, and, either simultaneously, before, or after, adding a test compound or plurality thereof;

measuring the amount of substrate cleaved in the presence of the test compound; and,

selecting test compounds that decrease ~~change~~ the amount of substrate cleaved compared to a control, thereby identifying ~~whereby test~~ compounds that inhibit the activity of the protease ~~polypeptide are candidate anti-tumor agents~~.

67. (Amended) The method of claim 65, wherein a plurality of the test compounds ~~substances~~ are screened simultaneously.

69. (Amended) A method for identifying compounds that inhibit the protease activity of the two-chain protease of claim 4 ~~a polypeptide~~, comprising:

contacting the two-chain protease ~~a polypeptide~~ of claim 4 with a substrate that is proteolytically cleaved by the protease ~~polypeptide~~, and, either simultaneously, before, or after, adding a test compound or plurality thereof;

measuring the amount of substrate cleaved in the presence of the test compound; and,

selecting test compounds that decrease ~~change~~ the amount of substrate cleaved compared to a control, thereby identifying ~~whereby test~~ compounds that inhibit the activity of the two-chain protease ~~polypeptide are candidate anti-tumor agents~~.

71. (Amended) The method of claim 67, wherein a plurality of the proteases ~~polypeptides~~ are linked to a solid support, either directly or via a linker.

72. (Amended) The method of claim 71, wherein the proteases ~~polypeptides~~ comprise an array.

73. (Amended) A method of identifying a compound that specifically binds to the protease of claim 1 or claim 5 ~~a single chain and/or two chain protease domain and/or to single or two chain full length polypeptide~~, comprising:

contacting the protease of claim 1 or claim 5 ~~a polypeptide~~ with a test compound or plurality thereof under conditions conducive to binding of the test compound to the protease ~~thereof~~;

measuring the amount of a test compound that remains bound to the protease; and,

selecting test compounds that remain bound to the protease compared to a control, thereby identifying compounds that specifically bind to the protease ~~polypeptide single chain protease domain, or two chain form thereof, the full length or two chain form of the full length polypeptide or compounds that inhibit binding of a compound known to bind to the polypeptide single chain protease domain or two chain form thereof or the two chain form of the full length polypeptide, wherein the known~~

~~compound is contacted with the polypeptide before, simultaneously with or after the test compound~~.

74. (Amended)) The method of claim 73, wherein the protease ~~polypeptide~~ is linked either directly or indirectly via a linker to a solid support.

76. (Amended) The method of claim 73, wherein a plurality of the test compounds ~~substances~~ are screened simultaneously.

77. (Amended) The method of claim 73, wherein a plurality of the proteases ~~polypeptides~~ are linked to a solid support.

78. (Amended) A method of identifying a compound that specifically binds to the two-chain protease of claim 4 ~~a single-chain and/or two-chain protease domain and/or to single or two-chain full-length polypeptide~~, comprising:

contacting the two-chain protease ~~a polypeptide~~ of claim 4 with a test compound or plurality thereof under conditions conducive to binding of the test compound to the protease ~~thereof~~;

measuring the amount of a test compound that remains bound to the protease; and,

selecting test compounds that remain bound to the protease compared to a control, thereby identifying compounds that specifically bind to the protease ~~polypeptide single-chain protease domain, or two-chain form thereof, the full-length or two-chain form of the full-length polypeptide or compounds that inhibit binding of a compound known to bind to the polypeptide single-chain protease domain or two-chain form thereof or the two-chain form of the full-length polypeptide, wherein the known compound is contacted with the polypeptide before, simultaneously with or after the test compound~~.

79. (Amended) A method for identifying activators of the zymogen form of the protease of claim 1 or claim 5 ~~an MTSP7~~, comprising:

contacting a zymogen form of the protease ~~polypeptide~~ of claim 1 or claim 5 with a substrate of the activated form of the protease ~~polypeptide~~;

adding a test compound, wherein the test compound is added before, after, or simultaneously with the addition of the substrate; and,

detecting cleavage of the substrate, thereby identifying compounds that activate the zymogen.

123. (Amended). A modified protease ~~polypeptide,~~ comprising the sequence of amino acids ~~acid residues~~ set forth between positions ~~as residues~~ 206-438 of ~~in~~ SEQ ID No. 16 ~~or polypeptide comprising the sequence of amino acid residues set forth as residues 206-438 in SEQ ID No. 16,~~ modified by the replacement of ~~except that~~ a free cysteine ~~residue in the recited sequence is replaced~~ with a serine ~~residue~~.

124. (Amended) The protease ~~A polypeptide~~ of claim 123 that consists of the sequence of amino acids ~~acid residues~~ set forth between positions ~~as residues~~ 206-438 of ~~in~~ SEQ ID No. 16 modified by the replacement of ~~in which~~ a free cysteine ~~residue in the recited sequence is replaced~~ with a serine ~~residue~~.

125. (Amended) A method for identifying compounds that inhibit the protease activity of the protease of claim 123 ~~a polypeptide,~~ comprising:

contacting the protease ~~a polypeptide of claim 123~~ with a substrate that is proteolytically cleaved by the protease ~~polypeptide~~, and, either simultaneously, before, or after, adding a test compound or plurality thereof;

measuring the amount of substrate cleaved in the presence of the test compound; and,

selecting test compounds that decrease the amount of substrate cleaved compared to a control, thereby identifying ~~wherein selected test~~ compounds that inhibit the activity of the protease ~~are candidate anti-tumor agents~~.

126 ~~125~~. (Amended) A conjugate~~,~~ comprising~~:~~ the protease ~~a polypeptide~~ of claim 123~~;~~ and a targeting agent linked to the protease ~~polypeptide~~ directly or via a linker.

127 ~~126~~. (Amended) A method for identifying compounds that inhibit the protease activity of the protease of claim 124 ~~a polypeptide,~~ comprising:

contacting the protease ~~a polypeptide of claim 123~~ with a substrate that is proteolytically cleaved by the protease ~~polypeptide~~, and, either simultaneously, before, or after, adding a test compound or plurality thereof;

measuring the amount of substrate cleaved in the presence of the test compound; and,

selecting test compounds that decrease the amount of substrate cleaved compared to a control, thereby identifying ~~wherein selected test~~ compounds that inhibit the activity of the protease ~~are candidate anti-tumor agents~~.

128 ~~127~~. (Amended) A conjugate~~,~~ comprising~~:~~ the protease ~~a polypeptide~~ of claim 124~~;~~ and a targeting agent linked to the protease ~~polypeptide~~ directly or via a linker.

Authorization for this examiner's amendment was given in a telephone interview with Stephanie L. Seidman, Ph.D., on 19 January 2006.

The following is an examiner's statement of reasons for allowance:

The examiner's amendment rejoins several claims withdrawn from examination but subject to rejoinder in accordance with the provisions of MPEP § 821.04 and amends the recitations of both previously examined claims and rejoined claims to ensure that the allowed method claims describe a specific protease and include a measuring or comparison step to state a complete method. The utility rejection of record of method

claims herein is withdrawn in view of the specification's disclosure that three specific cancer cell lines arising from different tissues express the MTSP7 protease at high levels. The threshold for utility is not high, and there is a specific and substantial utility in assays to find binding partners and inhibitors for the MTSP7 protease to establish the site(s) in cells of these cell lines where the protease, or its zymogen form reside(s) and its activity in the cells of these cell lines. It is also noted that binding partners, and inhibitors, of the protease may also be identified and selected in order to purify the useful protease from, e.g., a cell lysate or *in vitro* transcription/translation system. Claim 61 is restated in the examiner's amendment to more closely reflect the disclosure at pages 123-124 of the specification. The examiner's amendment rewrites claims 4 and 5 to avoid the disclosure of Alsobrook et al. by ensuring that proteases described by the amended claim do not comprise "a sequence" that may also be "a sequence" present in a protease of Alsobrook et al. The examiner's amendment also restates claims 50, 59, 65, 73 and 79 so that the methods of these claims, and of claims depending therefrom, may utilize the proteases of either claim 1 or claim 5, thus permitting allowance of claims 1, 2, 4, 5, 8, 9, 18, 19, 50-53, 59-61, 65-67, 69-79, 82, and 123-28 herewith.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is

571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
19 January 2006

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER